Cycles

Fig. 1: Verification of differential expression of HIF3alpha splice variant 1 by quantitative RT-PCR

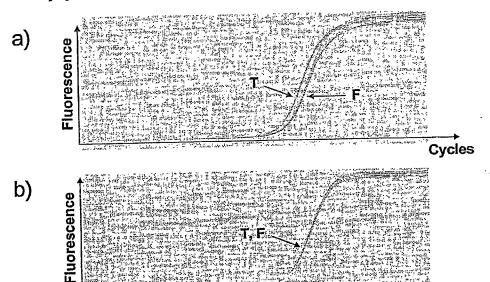
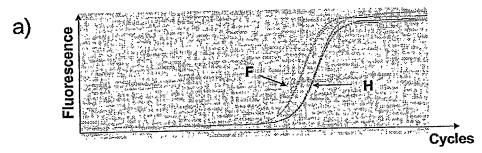


Fig. 2: Verification of differential expression of HIF3alpha splice variant 1 by quantitative RT-PCR



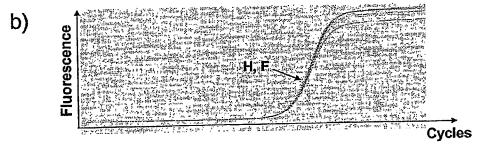
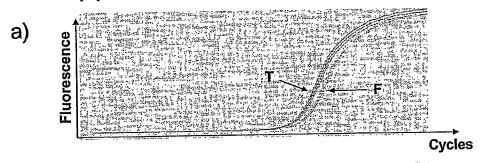
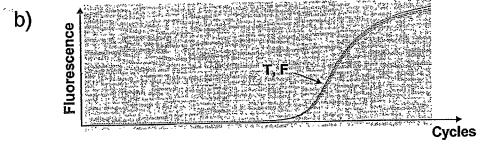


Fig. 3: Verification of differential expression of HIF3alpha splice variant 2 by quantitative RT-PCR





Cycles

Fig. 4: Verification of differential expression of HIF3alpha splice variant 3 by quantitative RT-PCR

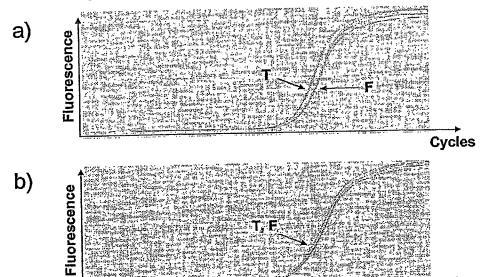
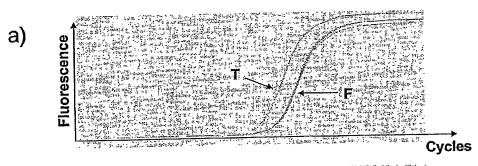


Fig. 5: Verification of differential expression of HIF3alpha splice variant 5 by quantitative RT-PCR



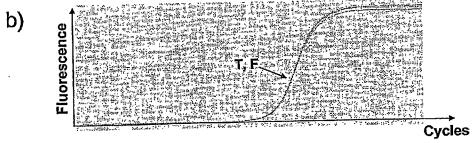


Fig. 6: SEQ ID NO. 1

Length: 289 bp

1 CATTTATGAG AGTTTATTCA TTCAAAACAT ATTTACTGTC GGGCGTGGTG
51 GTTCATACCA GTAATCCCAG CACTTTGGGA GGCCAAGGCA GGTGGATCGC
101 TTGAACTCAG GAGTTCAAGA CCAGCCTGGG CAACATGGTG GAACTTCGTC
151 TCTACAAAAC ATATAAACAT CAGCCAGGCA TGATGGCACA TAGCTGCAGT
201 CCCAGCTACT TGTGGGAGCT GAAGTAGGAG GATCACTTGA GCCCAGGAGG
251 TCGAGGCTGT GGTGAGCTGT GTTTGTGCCA CTGCACTCC

Alignment of SEQ ID NO. 1 with human HIF3alpha splice variant sv1 cDNA, Fig. 7: SEQ ID NO. 6

289	GGAGTGCAGTGGCACAAACACAGCTCACCACAGCCTCGACCTCCTGGGCT	240
	GGAGTGCAGTGGCACAAACACAGCTCACCGCAGCCTCGACCTCCTGGGCT	
	CAAGTGATCCTCCTACTTCAGCTCCCACAAGTAGCTGGGACTGCAGCTAT	
1471	CAAGTGATCCTCCTACTTCAGCTCCCACAAGTAGCTGGGACTGCAGCTAT	1520
189	GTGCCATCATGCCTGGCTGATGTTTATATGTTTTGTAGAGACGAAGTTCC	140
1521	GTGCCATCATGCCTGGCTGATGTTTATATGTTTTGTAGAGACGAGGTTTC	1570
139	ACCATGTTGCCCAGGCTGGTCTTGAACTCCTGAGTTCAAGCGATCCACCT	90
1.571	ACCATGTTGCCCCAGGCTGGTCTTGAACTCCTGAGTTCAAGCGATCCACCT	1620
89	GCCTTGGCCTCCCAAAGTGCTGGGATTACTGGTATGAACCACCACGCCCG	40
1621	GCCTTGGCCTCCCAAAGTGCTGGGATTACTGGTATGAACCACCACGCCCG	1670
	ACAGTAAATATGTTTTGAATGAATAAACTCTCATAAATG 1	
1671	ACAGTAAATATGTTTTGAATGAATAAACTCTCATAAATG 1709	

Figure 8: SEQ ID NO. 2: amino acid sequence of human HIF3alpha, splice variant 1

Length: 450 aa

-	MRPAAGAARR	PROCESMETR	CPSPAASAPT	WTRPLSCASP	SATCACTASA
٦.	PQLELIGHSI	FICCIDATE		TI.SPRKVEAP	TERCFSLRMK
51	POLELIGHSI	FDEIHLCDÖR	EPÖDVPTFFÖÖ	THOTALCOM	TO CERTIFIE OCT.
		**** *** ** TYTAT/プブブブ	MCCCHMRAYK	PPACIOPAGO	
TOT	STLTSRGRTL VLICEAIPHP	MILTITATION OF COLUMN	AUT CDUCT.DM	KETTYCDDRIA	EVAGYSPDDL
151	VLICEAIPHP	GSTEPPTGKG	WITTOWNSTITE	10 11 000000000000000000000000000000000	COCYT WTOTO
		ォイ かかかみなださだな	TUTTIJSKGUA	ATGOTIVETICAL	DOC
201	IGCSAYEYIH ATVVSGGRGP		ェスのヘンファマかんび	TOTTOTIOH	SRRPIORGAP
251	ATVVSGGRGP	Ö SESTAGAHE	TTPÖAFFTGA	110.552.2	GCDDT DDT T C
		OF DUDICIDE II.	ATTITOPSISE	AALAADPRKE	
30T	PILDGASVAA	DIDITOLAGE	DOCENT CADE D	THE TOTAL PROPERTY	HRIFTSGKDT
351	PILDGASVAA	TPSTPLATER	POSPLSADEP	DELLE AGETIM	#PARRED TV
	PILDGASVAA EAVETDLDIA	TM.I.TOTPORGO	NEPLGFHFVT	OSGVQWHKHS	SPOPRPPGUK
401	FAARLDIDTW	ODEDTERM	21,22,22	-	

Fig. 9: SEQ ID NO. 3:

amino acid sequence of
human HIF3alpha,
splice variant 2

Length: 342 aa

٦	MALGLORARS	TTELRKEKSR	DAARSRRSQE	TEVLYQLAHT	LPFARGVSAH
E7	TOKAGTMRIA	TSYLEMHRLC	AAGEWNQVGA	GGEPLDACYL	KALEGFVMVL
7.07	P.TVANCTOMAVI.S	ENVSKHTGUS	OLELIGHSIF	DFIHPCDQEE	TÖDYTJAĞĞI
751	TODENTAGES	FRCFSLRMKS	TLTSRGRTLN	LKAATWKVLN	CSGHMRAYKP
201	DAOTEDAGED	DSEPPLOCLV	LICEAIPHPG	SPERFFPRCKGW	LUSKRDIDMY
251	ETYCOOR TAE	VAGYSPDDLI	GCSAYEYIHA	LDSDAVSKSI	HJTPPRGÖWA
301	TGQYRFLARS	GGYLWTQTQA	TVVSGGRGPQ	SESIVCVHFL	IR

Fig. 10: SEQ ID NO. 4: amino acid sequence of human HIF3alpha, splice variant 3

Length: 632 aa

A 100 347
VSAH VMVL
ייייטטעד
PQQT
AYKP
LDMK
GQAV
TGVV
TGVV
LSEA
$D\Gamma D$
DDDF
PRLS
ששמט
SPEH

Fig. 11: SEQ ID NO. 5: amino acid sequence of human HIF3alpha, splice variant 5

Length: 648 aa

1 MRLTISYLRM	TOTAL CANAGEMENT	OVGAGGEPLD	ACYLKALEGF	VMVLTAEGDM
T WKPITSIFKM	TKIICAAGEMN	ZVOROGELEE	DODELODAL.T	POOTLSRRKV
51 AYLSENVSKH	LGLSQLELIG	HSTEDETHEC	DÖRRHÖDRUT	E O O TENTO
101 EAPTERCFSL		RTLNLKAATW	KVLNCSGHMR	AYKPPAQTSP
151 AGSPDSEPPL		PHPGSLEPPL		LDMKFTYCDD
201 RIAEVAGYSP	DDLTGCSAYE	YTHALDSDAV	SKSIHTLLSK	GQAVTGQYRF
		RGPQSESIVC	THURST. THUR	TGVVLSLEOT
251 LARSGGYLWT	Ö.T.ÖY.T.A ARGG		ATTITIOGATE	
301 EQHSRRPIQR	GAPSOKDTPN	PGDSLDTPGP		LSEAALAADP
	LLGPILDGAS	VAATPSTPLA	TRHPQSPLSA	DLPDELPVGT
221 KKECHIDEKK				DDDFQLNASE
401 ENVHRLFTSG	KDTEAVETDE			
451 OLPRAYHRPL	GAVPRPRARS	FHGLSPPALE	PSLLPRWGSD	PRLSCSSPSR
		SEDEDEGVEL	LGVRPPKRSP	SPEHENFLLF
	GARKRTLAQS			
551 PLSLSFLLTG	GPAPGSLQDP	TELTQFLLSV	PREATPOLIA	LGCAAPGLHA
		PSRHALTLTL	PHMFGAPGAP	SPLGWFAI
601 SPFSLPTISV	E ČINE TITTE E E Ö	T D	-	

Fig. 12: SEQ ID NO. 6: nucleotide sequence of human HIF3alpha cDNA, splice variant 1

Length: 1709 bp

1	ACTCGTAACT	CGCACCCGGG	TCCTGGCTGC	ACCGCATCCC	CTCCTGCACC
51	CCCTGGATGG	CCCTTCAGCC	AACGGGGGCC		TCGACCACGG
101	AGCTGCGCAA	GGAAAAGTCC	CGGGATGCGG	CCCGCAGCCG	GCGCAGCCAG
151	GAGACCGAGG	TGCTGTACCA	GCTGGCTCAC	ACGCTGCCCT	TCGCCCGCGG
201	CGTCAGCGCC	CACCTGGACA	AGGCCTCTAT	CATGCGCCTC	ACCATCAGCT
251	ACCTGCGCAT	GCACCGCCTC	TGCGCCGCAG	CTGGAGCTCA	TTGGACACAG
301	CATCTTTGAT	TTCATCCACC	CCTGTGACCA	AGAGGAGCTT	CAGGACGCCC
351	TGACCCCCCA	GCAGACCCTG	TCCAGGAGGA	AGGTGGAGGC	CCCCACGGAG
401	CGGTGCTTCT	CCTTGCGCAT	GAAGAGTACA	CTCACCAGCC	GCGGGCGCAC
451	CCTCAACCTC	AAGGCGGCCA	CCTGGAAGGT	GCTGAACTGC	TCTGGACATA
501	TGAGGGCCTA	CAAGCCACCT	GCGCAGACTT	CTCCAGCTGG	GAGCCCTGAC
551	TCAGAGCCCC	CGCTGCAGTG	CCTGGTGCTC	ATCTGCGAAG	CCATCCCCCA
601	CCCAGGCAGC	CTGGAGCCCC	CACTGGGCCG	AGGGGCCTTC	CTCAGCCGCC
651	ACAGCCTGGA	CATGAAGTTC	ACCTACTGTG	ACGACAGGAT	TGCAGAAGTG
701	GCTGGCTATA	GTCCCGATGA	CCTGATCGGC	TGTTCCGCCT	
751	CCACGCGCTG	GACTCCGATG	CGGTCAGCAA	GAGCATCCAC	
801	GCAAGGGCCA	GGCAGTAACA	GGGCAGTATC	GCTTCCTGGC	CCGGAGTGGT
851	GGCTACCTGT	GGACCCAGAC	CCAGGCCACA		GGGGACGGG
901	_CCCCCAGTCG	GAGAGTATCG	TCTGTGTCCA		AGCCAGGTGG
951	AAGAGACCGG	AGTGGTGCTG	TCCCTGGAGC		ACACTCTCGC
1001	AGACCCATTC	AGCGGGGCGC	CCCCTCTCAG	111001141040	CTAACCCTGG
1051	GGACAGCCTT	GACACCCCTG	GCCCCCGGAT	CCTTGCCTTC	CTGCACCCGC
1101	CTTCCCTGAG	CGAGGCTGCC	CTGGCCGCTG	ACCCCCGCCG	TTTCTGCAGC
1151	CCTGACCTCC	GTCGCCTCCT	GGGACCCATC		CTTCAGTAGC
1201	AGCCACTCCC	AGCACCCCGC	TGGCCACACG		AGTCCTCTTT
1251	CGGCTGATCT	CCCAGATGAA	CTACCTGTGG	GCACCGAGAA	
1301	CTCTTCACCT	CCGGGAAAGA	CACTGAGGCA		ATTTAGATAT
1351	AGCTCAGGAC	CCCAGCACCC	CACTCCTGAA		CCCCTGGGTT
1401	TTCACTTTGT	CACCCAGTCT	GGAGTGCAGT		CAGCTCACCG
1451	. CAGCCTCGAC	CTCCTGGGCT	CAAGTGATCC		GCTCCCACAA
1501	. GTAGCTGGGA	CTGCAGCTAT	GTGCCATCAT		TGTTTATATG
1551	TTTTGTAGAG		ACCATGTTGC	CCAGGCTGGT	CTTGAACTÇC TGGGATTACT
1601			GCCTTGGCCT		
1651	. GGTATGAACC	ACCACGCCCG	ACAGTAAATA	TGTTTTGAAT	GAATAAACIC
1701	. TCATAAATG				

Fig. 13: SEQ ID NO. 7: nucleotide sequence of human HIF3alpha cDNA, splice variant 2

Length: 2239 bp

1 TGGGAGCGGC GACTGGCGAG CCATGGCGCT GGGGCTGCAG CGCGCAAGGT 51 CGACCACGGA GCTGCGCAAG GAAAAGTCCC GGGATGCGGC CCGCAGCCGG 101 CGCAGCCAGG AGACCGAGGT GCTGTACCAG CTGGCTCACA CGCTGCCCTT 151 CGCCCGCGGC GTCAGCGCCC ACCTGGACAA GGCCTCTATC ATGCGCCTCA 201 CCATCAGCTA CCTGCGCATG CACCGCCTCT GCGCCGCAGG GGAGTGGAAC 251 CAGGTGGGAG CAGGGGGAGA ACCACTGGAT GCCTGCTACC TGAAGGCCCT 301 GGAGGGCTTC GTCATGGTGC TCACCGCCGA GGGAGACATG GCTTACCTGT 351 CGGAGAATGT CAGCAAACAC CTGGGCCTCA GTCAGCTGGA GCTCATTGGA 401 CACAGCATCT TTGATTTCAT CCACCCCTGT GACCAAGAGG AGCTTCAGGA 451. CGCCCTGACC CCCCAGCAGA CCCTGTCCAG GAGGAAGGTG GAGGCCCCCA 501 CGGAGCGGTG CTTCTCCTTG CGCATGAAGA GTACGCTCAC CAGCCGCGGG 551 CGCACCCTCA ACCTCAAGGC GGCCACCTGG AAGGTGCTGA ACTGCTCTGG 601 ACATATGAGG GCCTACAAGC CACCTGCGCA GACTTCTCCA GCTGGGAGCC 651 CTGACTCAGA GCCCCCGCTG CAGTGCCTGG TGCTCATCTG CGAAGCCATC 701 CCCCACCCAG GCAGCCTGGA GCCCCACTG GGCCGAGGGG CCTTCCTCAG 751 CCGCCACAGC CTGGACATGA AGTTCACCTA CTGTGACGAC AGGATTGCAG 801 AAGTGGCTGG CTATAGTCCC GATGACCTGA TCGGCTGTTC CGCCTACGAG 851 TACATCCACG CGCTGGACTC CGACGCGGTC AGCAAGAGCA TCCACACCTT 901 GCTGAGCAAG GGCCAGGCAG TAACAGGGCA GTATCGCTTC CTGGCCCGGA 951 GTGGTGGCTA CCTGTGGACC CAGACCCAGG CCACAGTGGT GTCAGGGGGA 1001 CGGGGCCCC AGTCGGAGAG TATCGTCTGT GTCCATTTTT TAATCAGGTA 1051 AGCAGGAGGA GGGGCTGGGG TGGCTGTGT TGGGCCTGAT CTGCATGTGT 1101 GGACAGGTGT GTGTGTGTGT GTGTGTGTGT GCGTATGAGC 1151 ATGCATGTGT ATCATGCATA AGTGTATGTG AGGGAGTGTG CACGTGTACA 1201 CATATGAGGA ATGTGTGTCA CCATGTAAAT GCCGGTGTGT GTGTCTGCAT 1301 TTTTTTGCG TGAACCTCTG CTTAAGTGGA TTGTTAATTC AAATTAGAAA 1351 GGGGTCTTTA TTTGGCCTGG CATGGTGGCT CATGCCTGTA ATCCTAGCAC 1401 TTTGGGAGGC TGAGGTGGGC GGATTGCCTG AGCTCAGGAG TTCGAAACCA 1451 GCCTGGGCAA CATGACGAAA TGCTGTTTCT GCTAATAATA CCAAAAATTA 1501 GCCGGGTGTG GTGACACATG CCTGTGATCC CAACTACTCG GGAGGCTGAG 1551 GCACGAGAAT CATTAGAACC CGGGTGGTGG AGGCTGCAGT GAGCCGAGAT 1601 TGCGTCAGTG CACTCTGGCC TCGGCAACAG AGCGAGACTC TGTCTCAAAC 1651 AAACAAACAA ACAAACAAAA GGACTCTATA TTCAAGTTAA AATAAGAAGT 1701 GTAACAGAAT CATGGGGTCT TTTTTGCTTT TTAAATTTTG ATGTGGCTCA 1751 CGCCTGTAAA TCCCAAGGTG TTGGGATTAC AGGCGTGAGC CACTGCACCC 1801 GGCCCATGTT GTGGTTTATA TCAGTAGTTC CTTTGTAAAT AGTGAACAGT 1851 ATTCCATGGT ATGAATAGAG CACAGTTTTT TTTTTTATCC ATTCACCAGT 1901 TAGAAGACAT TGGGCTGTTT CCAAGTTTGG GTGATTACAA AAAACAGCTA 1951 CTGTAAACAT TCTCATACAA GATTTTATGA GATCACATGT TTTCATTTCT 2001 CTTGGGTAAA CAGCTAGGAT TGGAATGGAT GGGTTATATA GTAAGTGTAT 2051 ATTTAATCTA AGAAACTGCC ATGGCTGGGC ACAGTGGCTC ACGCCTGTAA

2101 TCCCAGTACT TTGGGAAGCC AAGGAAGGAG GATGACTAGA GCCTCTGAGG 2151 TGAAGACCAG CCTGGGCAAA GTGGTTAAGA CTCAACCGCA AAAAAAGAAA

2201 AACAGAAAAC CTGAAAACAA ACCAAAAAAA AAAAAAAAA

Figure 14: SEQ ID NO. 8: nucleotide sequence of human HIF3alpha cDNA, splice variant 3

Length: 2082 bp

1	GACTGGCGAG	CCATGGCGCT	GGGGCTGCAG	CGCGCAAGGT	CGACCACGGA
51		GAAAAGTCCC	GGGATGCGGC	CCGCAGCCGG	CGCAGCCAGG
101	AGACCGAGGT	GCTGTACCAG	CTGGCTCACA	CGCTGCCCTT	CGCCCGCGGC
151	GTCAGCGCCC	ACCTGGACAA	GGCCTCTATC	ATGCGCCTCA	CCATCAGCTA
201	CCTGCGCATG	CACCGCCTCT	GCGCCGCAGG	GGAGTGGAAC	CAGGTGGGAG
251	CAGGGGGAGA	ACCACTGGAT	GCCTGCTACC	TGAAGGCCCT	GGAGGGCTTC
301	GTCATGGTGC	TCACCGCCGA	GGGAGACATG	GCTTACCTGT	CGGAGAATGT
351	CAGCAAACAC	CTGGGCCTCA	GTCAGCTGGA	GCTCATTGGA	CACAGCATCT
401	TTGATTTCAT	CCACCCTGT	GACCAAGAGG	710 0 X Z 0====	CGCCCTGACC
451	CCCCAGCAGA	CCCTGTCCAG	GAGGAAGGTG	GAGGCCCCCA	
501	CTTCTCCTTG	CGCATGAAGA	GTACGCTCAC	CAGCCGCGGG	
551	ACCTCAAGGC	GGCCACCTGG	AAGGTGCTGA	ACTGCTCTGG	
601	GCCTACAAGC	CACCTGCGCA	GACTTCTCCA	GCTGGGAGCC	
651	GCCCCCGCTG	CAGTGCCTGG	TGCTCATCTG	CGAAGCCATC	CCCCACCCAG
701	GCAGCCTGGA	GCCCCCACTG	GGCCGAGGGG	CCTTCCTCAG	
751	CTGGACATGA	AGTTCACCTA	CTGTGACGAC	AGGATTGCAG	
801	CTATAGTCCC	GATGACCTGA	TCGGCTGTTC	CGCCTACGAG	TACATCCACG
851	CGCTGGACTC	CGACGCGGTC	AGCAAGAGCA	TCCACACCTT	GCTGAGCAAG
901	GGCCAGGCAG	TAACAGGGCA	GTATCGCTTC	CTGGCCCGGA	
951	CCTGTGGACC	CAGACCCAGG	CCACAGTGGT	GTCAGGGGGA	CGGGGCCCCC
1001	AGTCGGAGAG	TATCGTCTGT	GTCCATTTTT	TAATCAGCCA	GGTGGAAGAG
1051	ACCGGAGTGG	TGCTGTCCCT	GGAGCAAACG	GAGCAACACT	CTCGCAGACC
1101	CATTCAGCGG	GGCGCCCCT	CTCAGAAGGA	CACCCCTAAC	CCTGGGGACA
1151	GCCTTGACAC	CCCTGGCCCC	CGGATCCTTG	CCTTCCTGCA	
1201	CTGAGCGAGG	CTGCCCTGGC	CGCTGACCCC	CGCCGTTTCT	GCAGCCCTGA
1251	CCTCCGTCGC	CTCCTGGGAC	CCATCCTGGA		GTAGCAGCCA
1301	CTCCCAGCAC	CCCGCTGGCC	ACACGGCACC	CCCAAAGTCC	
1351	GATCTCCCAG	ATGAACTACC			
1401	CACCTCCGGG	AAAGACACTG	AGGCAGTGGA		GATATAGCTC
1451	AGGATGCTGA	TGCTCTGGAT	TTGGAGATGC		CATCTCCATG
1501	GATGATGACT	TCCAGCTCAA			GGGCCTACCA
1551	CAGACCTCTG	GGGGCTGTCC			
1601	TGTCACCTCC	AGCCCTTGAG			
1651	CCCCGGCTGA	. GCTGCTCCAG	CCCTTCCAGA		
1701	TCCCATGGCT	GGGGCTCGGA	, agaggaccct		
1751	AGGACGAGGG	AGTGGAGCTG			
1801	AGCCCAGAAC	ACGAAAACTI			
1851					
1901	CTGTTTTATA	GATAGGAAAC			
1951	TACAGAAAGT	CAGTGGGCCA			
2001	ACTAATGGGT				CGCCACTGCA
2051	CCCCAGCATG	AGCGACAGAA	TGGGACCTTG	TC	

Figure 15: SEQ ID NO. 9: nucleotide sequence of human HIF3alpha cDNA, splice variant 5

Length: 2595 bp

1	AACTCGCACC	CGGGTCCTGG	CTGCACCGCA	TCCCCTCCTG	CACCCCCTGG
51	Δ madacacamina	ACCCAACGGG	GGCCTGGGCG	ATGGTCGACC	WCGGWGCIGC
101	GCAAGGAAAA	GTCCCGGGAT	GCGGCCCGCA	GCCGGCGCAG	CCAGGAGACC
151	GAGGTGCTGT	ACCAGCTGGC	TCACACGCTG	CCCTTCGCCC	GCGGCGTCAG
201	CGCCCACCTG	GACAAGGCCT	CTATCATGCG	CCTCACCATC	
251	GCATGCACCG	CCTCTGCGCC	GCAGGGGAGT		GGGAGCAGGG
301	GGAGAACCAC	TGGATGCCTG	CTACCTGAAG	GCCCTGGAGG	GCTTCGTCAT
351			ACATGGCTTA	${\tt CCTGTCGGAG}$	
401	AACACCTGGG	CCTCAGTCAG	CTGGAGCTCA	${\tt TTGGACACAG}$	CATCTTTGAT
451	TTCATCCACC	CCTGTGACCA	AGAGGAGCTT	CAGGACGCCC	
501	GCAGACCCTG	TCCAGGAGGA	AGGTGGAGGC	CCCCACGGAG	
551			CTCACCAGCC	GCGGGCGCAC	CCTCAACCTC
601		CCTGGAAGGT	GCTGAACTGC		TGAGGGCCTA
651	CAAGCCACCT	GCGCAGACTT	CTCCAGCTGG	GAGCCCTGAC	
701	CGCTGCAGTG		ATCTGCGAAG		CCCAGGCAGC
751	CTGGAGCCCC		AGGGGCCTTC		ACAGCCTGGA
801	CATGAAGTTC			TGCAGAAGTG	GCTGGCTATA
851	GTCCCGATGA			ACGAGTACAT	
	GACTCCGACG			ACCTTGCTGA	GCAAGGGCCA
901 951	GGCAGTAACA				
951 1001				GGGGACGGGG	
	GAGAGTATCG				AAGAGACCGG
1051				ACACTCTCGC	AGACCCATTC
1101					GGACAGCCTT
1151					CTTCCCTGAG
1201	~				CCTGACCTCC
1251					AGCCACTCCC
1301				AGTCCTCTTT	CGGCTGATCT
1351					
1401				ATTTAGATAT	AGCTCAGGAT
1451					
1503					TACCACAGAC
1551					TGGCCTGTCA
1603					GTGACCCCCG
1651		C-TCCAGCCCT			
170					GGACGAGGAC
175:				-	
180:	L GAGGGAGTG			•	
1.85	AGAACACGA	A AACTTTCTG		-	
190		C AGCCCCAGG			
195				C ATTCTCATTC	-
200					
205					GTCCCTCACC
210	1 CTTACCTTG	A CTTTACCCC	W CWIGITIGG	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	

27 57	CCTTGGGTGG	TTTGCAATCT	${\tt GAAGACTTCT}$	CCAGCCACAC	AGGCACATGC
27.03	y Cy CCCy CCC	TACTACTACT	ATATTGCCAG	GTGGGGAGAG	AAGCCAGGAC
2201	CACORCA CORC	שרייים כריא ריכיא מיים ביים ביים ביים ביים ביים ביים ביים	TCTATGTGCC	TCCCTTACCC	CCCAGCTTTC
2251	CCCTCAGCIG	TCTGCCWCCW	CTTGGTCTCC	CACAGGAAAA	GGCCTCCCCC
23 01	TTTCTACAGA	1GGIGCIACI	CGTTTGTGGA	ACCCACTCCT	CGCTCTGTTT
2351	CTTCTTAGCC	CCATTTACCC	CGITIGIGG	שאיזים ממממממממ שאיזים ממממממממ	ጥርጥሮልሮርሮርጥ
2401	TGTCAGAGAG	TGGCCTATCC	AGATTGGTGC	TATGGGGGGG	ርአ አጥጥርጥር ርጥ
2451	CCCTCCTCCC	TCTGGAGGTG	ATGTGGGCCC	TCAAIGGAGG	GWWIIGIGGT
2501	GGGCTAGGGA	AAGGGGAGGG	ACTAGACTGG	CCACACTGGC	ICIGHMACIC
2551	ACCAALCTCT	ATACACCATA	AAGACCTCAC	CTTGGTAGGC	ACCAG

Fig. 16: SEQ ID NO. 10:

nucleotide sequence of human
HIF3alpha splice variant 1
coding sequence

Length: 1353 bp

1	ATGCGGCCCG	CAGCCGGCGC	AGCCAGGAGA	CCGAGGTGCT	GTACCAGCTG
51		TGCCCTTCGC		AGCGCCCACC	TGGACAAGGC
101	CTCTATCATG			GCGCATGCAC	CGCCTCTGCG
151	CCGCAGCTGG	AGCTCATTGG	ACACAGCATC	TTTGATTTCA	
201	TGACCAAGAG	GAGCTTCAGG	ACGCCCTGAC	CCCCCAGCAG	
251	GGAGGAAGGT	GGAGGCCCCC	ACGGAGCGGT	GCTTCTCCTT	
301	AGTACACTCA	CCAGCCGCGG	GCGCACCCTC	AACCTCAAGG	
351	GAAGGTGCTG	AACTGCTCTG	GACATATGAG	000011101110	CCACCTGCGC
401	AGACTTCTCC	AGCTGGGAGC	CCTGACTCAG	AGCCCCCGCT	
451	GTGCTCATCT	GCGAAGCCAT	CCCCCACCCA		
501	GGGCCGAGGG	GCCTTCCTCA	GCCGCCACAG	CCTGGACATG	
551	ACTGTGACGA	CAGGATTGCA	GAAGTGGCTG		CGATGACCTG
601	ATCGGCTGTT	CCGCCTACGA	GTACATCCAC		CCGATGCGGT
651	CACCAACACC	A TCCACACCT	TGCTGAGCAA	GGGCCAGGCA	GTAACAGGGC
701	AGTATCGCTT	CCTGGCCCGG	AGTGGTGGCT	ACCTGTGGAC	CCAGACCCAG
751	GCCACAGTGG		ACGGGGCCCC	CAGTCGGAGA	GTATCGTCTG
801	TGTCCATTTT	TTAATCAGCC	AGGTGGAAGA	GACCGGAGTG	
851	TGGAGCAAAC	GGAGCAACAC	TCTCGCAGAC		GGGCGCCCC
901	TCTCAGAAGG	ACACCCCTAA	CCCTGGGGAC	AGCCTTGACA	CCCCTGGCCC
951	CCGGATCCTT	GCCTTCCTGC	ACCCGCCTTC	CCTGAGCGAG	GCTGCCCTGG
1001	CCGCTGACCC	CCGCCGTTTC	TGCAGCCCTG		
1051	CCCATCCTGG	ATGGGGCTTC	AGTAGCAGCC		
1101	CACACGGCAC	CCCCAAAGTC	CTCTTTCGGC		GATGAACTAC
1151		CGAGAATGTG			
1201		AGACAGATTT			GCACCCCACT
1251		AATGAGCCCC			CAGTCTGGAG
1301		CAAACACAGC		CTCGACCTCC	TGGGCTCAAG
1351	TGA				
1001	7				

Fig. 17: SEQ ID NO. 11: nucleotide sequence of human HIF3alpha splice variant 2 coding sequence

Length: 1029 bp

_	ATGGCGCTGG	aaamaaxaaa	CCCAACCTCC	ACCACGGAGC	TGCGCAAGGA
1			GCAGCCGGCG	CAGCCAGGAG	ACCGAGGTGC
51	AAAGTCCCGG			CCCGCGGCGT	
101	TGTACCAGCT	GGCTCACACG	CTGCCCTTCG		
151	CTGGACAAGG	CCTCTATCAT		ATCAGCTACC	
201	CCGCCTCTGC	GCCGCAGGGG	AGTGGAACCA	GGTGGGAGCA	
251	CACTGGATGC	CTGCTACCTG	AAGGCCCTGG	AGGGCTTCGT	
301	ACCGCCGAGG	GAGACATGGC	TTACCTGTCG	GAGAATGTCA	GCAAACACCT
351		CAGCTGGAGC	TCATTGGACA	CAGCATCTTT	GATTTCATCC
	ACCCCTGTGA		CTTCAGGACG	CCCTGACCCC	CCAGCAGACC
401				GAGCGGTGCT	TCTCCTTGCG
451	CTGTCCAGGA		GCCGCGGGCG		CTCAAGGCGG
501	CATGAAGAGT				CTACAAGCCA
551	CCACCTGGAA		TGCTCTGGAC		CCCCGCTGCA
601	CCTGCGCAGA		TGGGAGCCCT		
651	GTGCCTGGTG	CTCATCTGCG			AGCCTGGAGC
701	CCCCACTGGG	CCGAGGGGCC	TTCCTCAGCC		GGACATGAAG
7,51	TTCACCTACT	GTGACGACAG	GATTGCAGAA		ATAGTCCCGA
801	TGACCTGATC		CCTACGAGTA		CTGGACTCCG
851	ACGCGGTCAG			TGAGCAAGGG	CCAGGCAGTA
	ACAGGGCAGT			GGTGGCTACC	TGTGGACCCA
901					TCGGAGAGTA
951	GACCCAGGCC			000000	
1001	TCGTCTGTGT	CCATTTTTA	HICHGGIMM		

Fig. 18: SEQ ID NO. 12:

nucleotide sequence of human
HIF3alpha splice variant 3
coding sequence

Length: 1899 bp

_	**************************************	GGCTGCAGCG	CGCAAGGTCG	ACCACGGAGC	TGCGCAAGGA
1		GATGCGGCCC	GCAGCCGGCG	CAGCCAGGAG	
51	HANGICCCGG	GGCTCACACG		CCCGCGGCGT	CAGCGCCCAC
101				ATCAGCTACC	TGCGCATGCA
151	CIGGACAAGG	GCCGCAGGGG		GGTGGGAGCA	GGGGGAGAAC
201		CTGCTACCTG	AAGGCCCTGG	AGGGCTTCGT	CATGGTGCTC
251		GAGACATGGC	TTACCTGTCG	GAGAATGTCA	GCAAACACCT
301		CAGCTGGAGC	TCATTGGACA	CAGCATCTTT	GATTTCATCC
351		CCAAGAGGAG	CTTCAGGACG	CCCTGACCCC	CCAGCAGACC
401		GGAAGGTGGA	GGCCCCCACG	GAGCGGTGCT	TCTCCTTGCG
451		ACGCTCACCA		CACCCTCAAC	CTCAAGGCGG
501		GGTGCTGAAC	TGCTCTGGAC	ATATGAGGGC	CTACAAGCCA
551		CTTCTCCAGC	TGGGAGCCCT	GACTCAGAGC	CCCCGCTGCA
601		CTCATCTGCG	AAGCCATCCC	CCACCCAGGC	AGCCTGGAGC
651		CCGAGGGGCC	TTCCTCAGCC	GCCACAGCCT	GGACATGAAG
701				GTGGCTGGCT	ATAGTCCCGA
751	TTCACCTACT		CCTACGAGTA	CATCCACGCG	CTGGACTCCG
801		GGCTGTTCCG	CACACCTTGC	TGAGCAAGGG	
851		CAAGAGCATC	GGCCCGGAGT	GGTGGCTACC	
901		ATCGCTTCCT	CAGGGGGACG	GGGCCCCCAG	
951		ACAGTGGTGT CCATTTTTA	ATCAGCCAGG	TGGAAGAGAC	
1001	TCGTCTGTGT	• • • • • • • • • • • • • • • • • • •	GCAACACTCT		TTCAGCGGGG
1051		AGCAAACGGA	CCCCTAACCC		CTTGACACCC
1101		CAGAAGGACA	TTCCTGCACC		
1151		GATCCTTGCC		•••	·
1201		CTGACCCCCG			
1251		ATCCTGGATG	CAAAGTCCTC		
1301		ACGGCACCCC			
1351		TGGGCACCGA			
1401		GCAGTGGAGA			
1451		GGAGATGCTG			
1501		CCAGCGAGCA			
1551		CGGCCCCGTG			
1601		CTCCCTGCTA			
1651		CTTCCAGAGG			
1701		AGGACCCTGG			
1751		r gggagtgaga			
1801		C TGCTCTTTCC			
1851	GATTCTCTG	G CCCTCATTAC	CTAGCTGGCT	TAAACCTACT	: GTTTTATAG

WO 2005/059562 PCT/EP2004/053573 21/46

Fig. 19: SEQ ID NO. 13:
 nucleotide sequence of human
 HIF3alpha splice variant 5
 coding sequence

Length: 1947 bp

1	አመረረረረር መደረ	ССАТСАССТА	CCTGCGCATG	CACCGCCTCT	GCGCCGCAGG
51	ATGCGCCTCW	CAGGTGGGAG	CAGGGGGAGA	ACCACTGGAT	GCCTGCTACC
101	TGAAGGCCCT	GGAGGGCTTC		TCACCGCCGA	GGGAGACATG
151		CGGAGAATGT	CAGCAAACAC		GTCAGCTGGA
201			TTGATTTCAT		GACCAAGAGG
251			CCCCAGCAGA		GAGGAAGGTG
301	AGCTICAGGA		CTTCTCCTTG		
351	CACCCCCCC	CGCACCCTCA	ACCTCAAGGC	GGCCACCTGG	AAGGTGCTGA
401	ACTOCTOTO	ACATATGAGG	GCCTACAAGC	CACCTGCGCA	GACTTCTCCA
451	CCTCCCACCC	CTGACTCAGA	GCCCCGCTG	CAGTGCCTGG	TGCTCATCTG.
501	CCAACCCATC	CCCCACCCAG	GCAGCCTGGA	GCCCCCACTG	GGCCGAGGGG
551	CGAAGCCAIC	CCGCCACAGC	CTGGACATGA	AGTTCACCTA	CTGTGACGAC
601	ACCATTCCTCAG	AAGTGGCTGG	CTATAGTCCC	GATGACCTGA	TCGGCTGTTC
651	CCCCTACCAC	TACATCCACG	CGCTGGACTC	CGACGCGGTC	AGCAAGAGCA
701	TCCACACCTT	GCTGAGCAAG	GGCCAGGCAG	TAACAGGGCA	GTATCGCTTC
751	CTCCCCCCCGA	GTGGTGGCTA	CCTGTGGACC	CAGACCCAGG	CCACAGTGGT
801	CTCACCCCGA	CGGGGCCCCC	AGTCGGAGAG	TATCGTCTGT	GTCCATTTTT
851	TANTCACCCA	GGTGGAAGAG	ACCGGAGTGG	TGCTGTCCCT	GGAGCAAACG
901	GAGCAACACT	CTCGCAGACC	CATTCAGCGG	GGCGCCCCT	CTCAGAAGGA
951	CACCCCTAAC		GCCTTGACAC	CCCTGGCCCC	CGGATCCTTG
1001		CCCGCCTTCC			
1051	CGCCGTTTCT	GCAGCCCTGA	CCTCCGTCGC	CTCCTGGGAC	CCATCCTGGA
1101		GTAGCAGCCA		CCCGCTGGCC	ACACGGCACC
1151		TCTTTCGGCT	GATCTCCCAG	ATGAACTACC	TGTGGGCACC
1201		ACAGACTCTT		AAAGACACTG	AGGCAGTGGA
1251		GATATAGCTC		TGCTCTGGAT	
1301		CATCTCCATG			CGCCAGCGAG
1351	CAGCTACCCA	GGGCCTACCA	CAGACCTCTG		CCCGGCCCCG
1401		TTCCATGGCC	TGTCACCTCC	AGCCCTTGAG	CCCTCCCTGC
1451		GGGGAGTGAC			CCCTTCCAGA
1501	GGGGACCCCT				AGAGGACCCT
1551	GGCCCAGAGC	TCAGAGGACG	AGGACGAGGG		CTGGGAGTGA
1601	GACCTCCCAA	AAGGTCCCCC	: AGCCCAGAAC		TCTGCTCTTT
1651	CCTCTCAGCC				CAGGGAGCCT
1701	GCAGGACCCC	ACTGAACTTA	CCCAATTCCT		TTAAGTTTTC
1751	CCATTCTAGA	CCCCTACCCT	CTAGGCTGTG	CTGCTCCTGG	ACTICATGCC
1801	TCTCCATTCT				
1851	CCCACCCCAC		ATGCACTTAC		
1901	TTGGGGCACC		: TCACCCCTTG	GGTGGTTTGC	AATCTGA

Fig. 20: Schematic assembly of SEQ ID NO. 6, with human ESTs and human mRNA (AK021421)

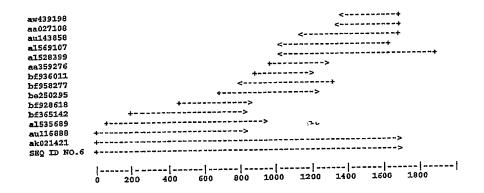


Fig. 21: Schematic assembly of SEQ ID NO. 7, with human ESTs and human mRNA (BCO26308)

```
ai039141
au145315
aa371.675
bf958277
be250295
bf928618
bf365142
al535689
al519496
al528423
bc026308
bg99633
al541807
au118510
bd7721.09
SEQ ID NO.7
```

Fig. 22: Schematic assembly of SEQ ID NO. 8, with human ESTs and human mRNAs (AK021421, AK021653, AK027725, AB054067, AF463492)

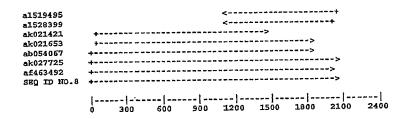


Fig. 23: Schematic assembly of SEQ ID NO. 9, with human ESTs and human mRNA (AKO 21653)

```
a1091960
aa706005
aw270837
                                                <----+
<----+
b£439358
ai306123
ai281985
                                               <-----+
ai697524
aw044635
au145056
                                             <-----+
<-----+
aw960466
bm972872
                                             <-----
bq185343
bm971722
                                          ------>
+----->
bq188179
bm727831
h78554
                                       +---->
+---->
bq722091
ai133319
bi058319
r56537
                                      +---->
aul19436 +----->
sk021653 +----->
skQ ID NO.9 +----->
```

Fig. 24: Identification of differentially expressed genes by microarray hybridization

Biochip	Type of probe	Used probes (Cy5-/Cy3-labeled)	Ratio fluorescence intensity: temporal / frontal cortex		
		PT _{SSH(2)} / PF _{SSH(1)}	1.40		
- 1	В	PT/PF	1.19		
	A	PT/PF	0.65		
4	С	PT _{SSH(4)} / CT _{SSH(3)}	0.65		
. 7	В	CF/PF	0.95		

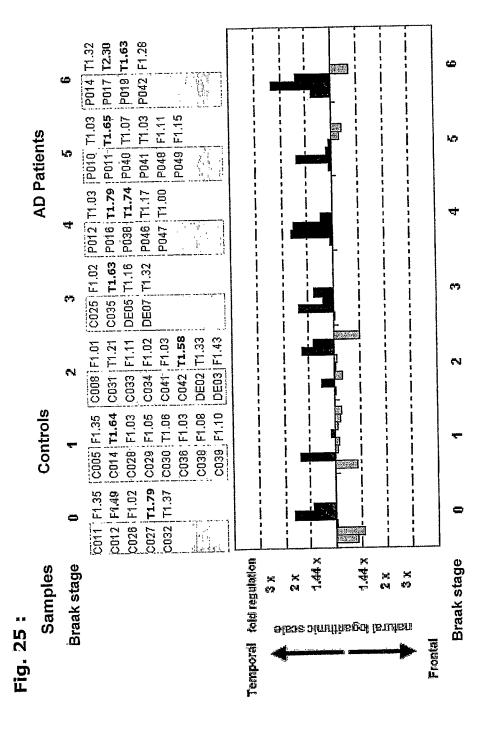
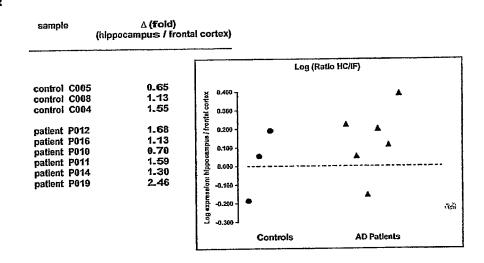
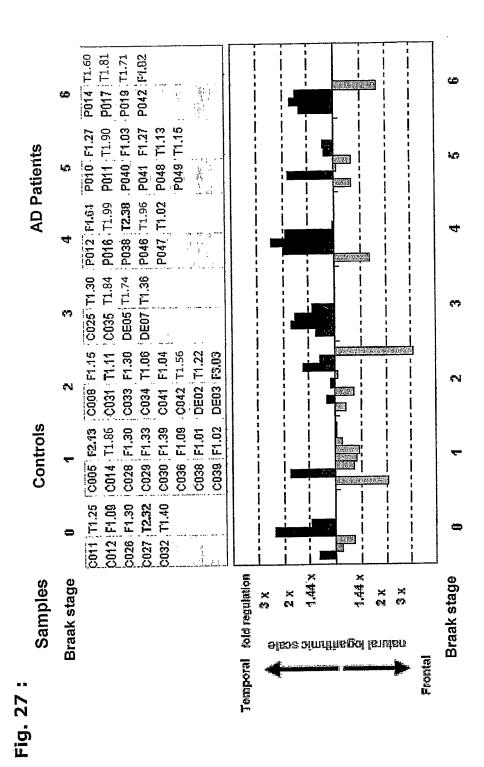
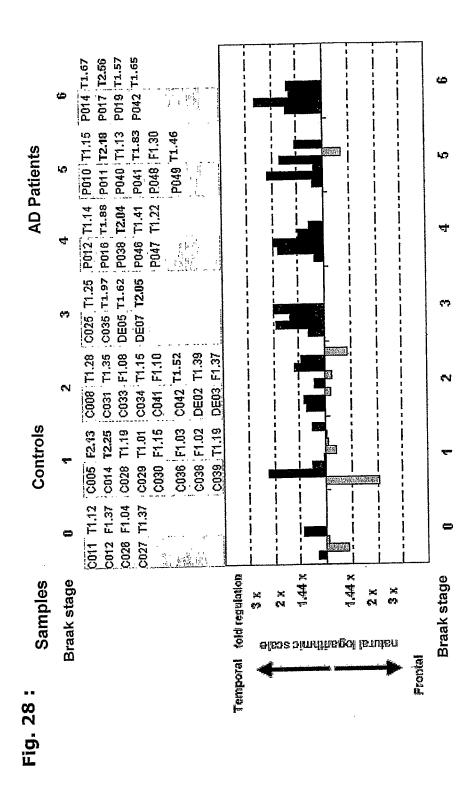


Fig. 26:

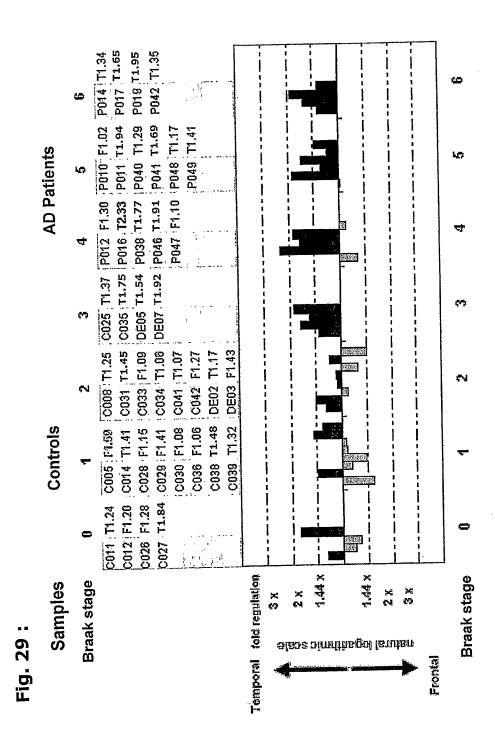




SUBSTITUTE SHEET (RULE 26)

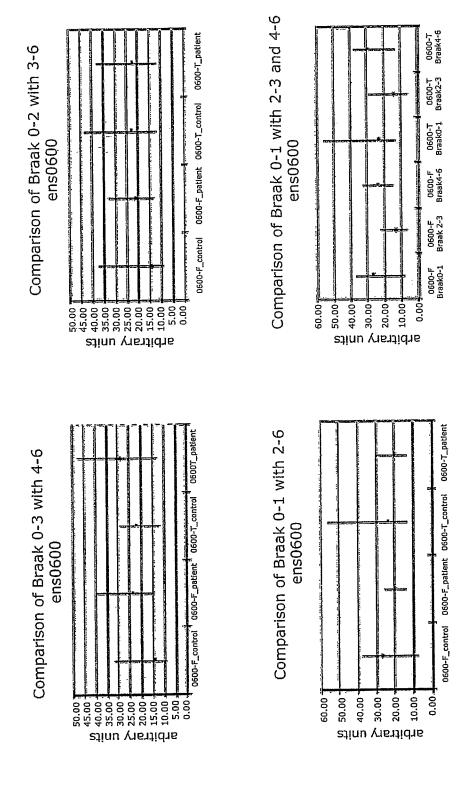


SUBSTITUTE SHEET (RULE 26)

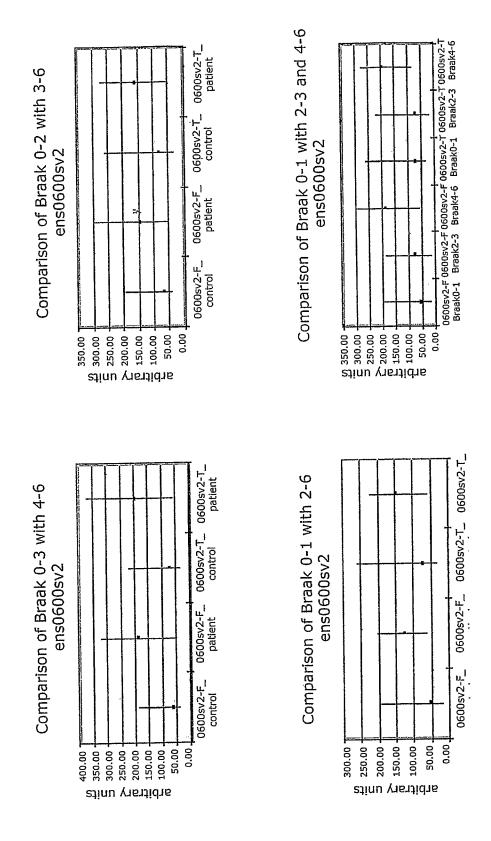


SUBSTITUTE SHEET (RULE 26)

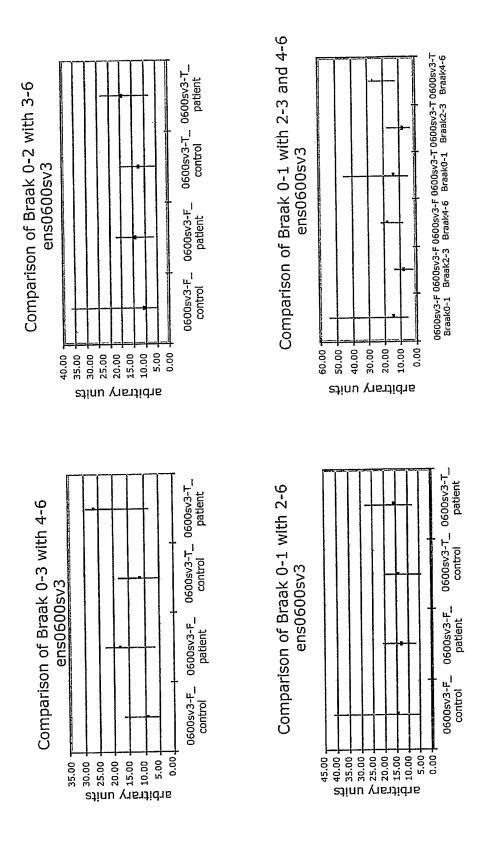
expression of HIF3alpha splice variant 1 Fig. 30: Analysis of absolute mRNA



expression of HIF3alpha splice variant 2 Fig. 31: Analysis of absolute mRNA



expression of HIF3alpha splice variant 3 Fig. 32: Analysis of absolute mRNA



expression of HIF3alpha splice variant 5 Fig. 33: Analysis of absolute mRNA

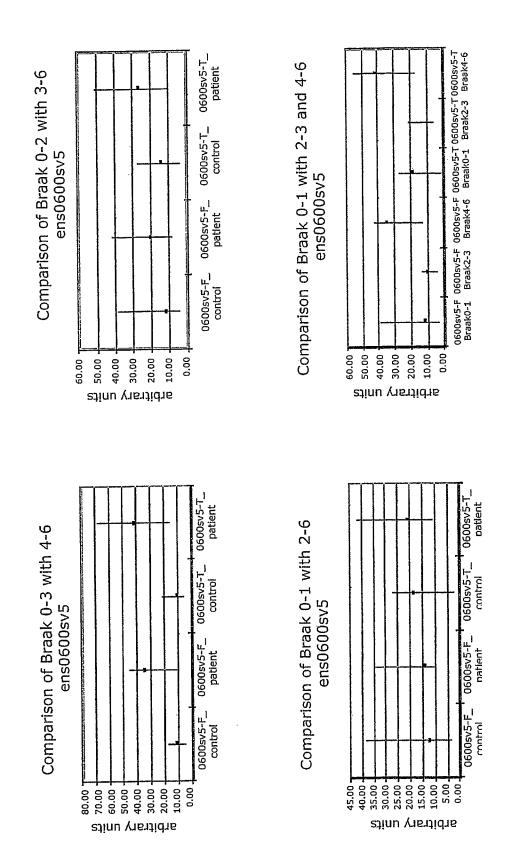
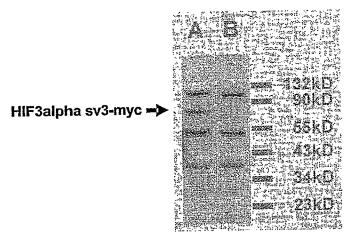


Fig. 34: Western Blot of H4APPsw cell protein extracts labeled with anti-HIF3alpha sv3-myc antibodies



PCT/EP2004/053573

Fig. 35: Immunofluorescence analysis of HIF3alpha sv3 protein in neuroglioma cells

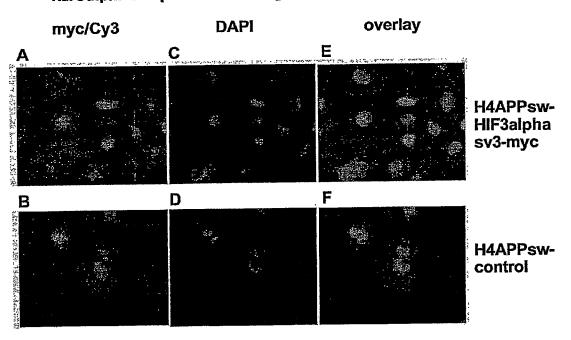


Fig. 36: Images of human brain sections labeled with anti-HIF3a antiserum, cell specific markers and DAPI

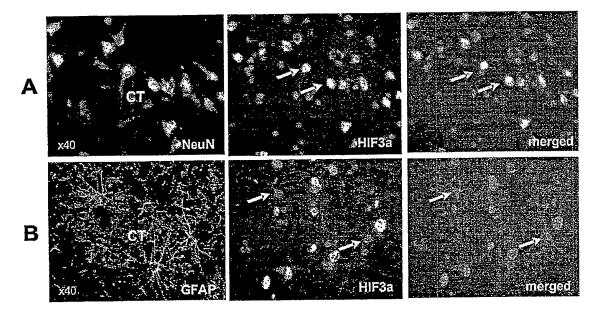


Fig. 37: Images of human brain sections labeled with anti-HIF3a antiserum, cell specific markers and DAPI

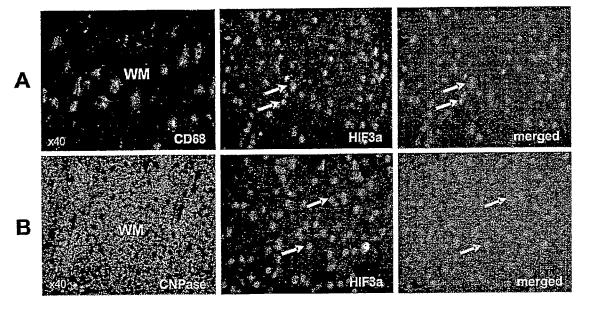


Fig. 38: Images of human brain sections labeled with anti-HIF3a antiserum, GFAP and DAPI

Control (Braak 1)	Control (Braak 3)	Patient (Braak 4)	Patient (Braak 5)	Patient (Braak 6)	
erf of	CF	CF.	CF	G.F.	
3/40					
	CT .	a a		oī.	
vig.	ا ک چین چین				

Fig. 39: Expression level of HIF3a sv3 expressing transgenic flies

name	cycle number	mean	stdev	error %	factor [normalization to rp49 cycle number]	mean*factor	difference	expression normalized to housekeeping gene and efficiency of HIF3a-sv3 primer	
HIF3a-sv3#3	30.03	30.237	0.2155	0.71265776	1	30.2366667			
HIF3a-sv3#3	30.22								HIF3a-sv3#3 is 2.8 times higher
HIF3a-sv3#3	30.46								expressed than HIF3a-sv3#4
					<u> </u>				<u></u>
HIF3a-sv3#4	30.96	31.160	0.1778	0.67048745	1.010625536	31.4910917	-1.25442502	-2.847544799	1
HIF3a-sv3#4	31.22								!
HIF3a-sv3#4	31.30								
HIF3a-sv3#57		27.953	0.1060	0.37915843	1.043347488	29.1650401	1.07162656	2.432592298	HIF3a-6v3#57 is 2,4 times higher
HIF3a-sv3#57	27.97								expressed than HIF3a-sv3#3 and 5.3
HIF3a-sv3#5	28.05						-2.32605158	-5.280137096	times higher than HiF3a-sv3#4

E= 10^(-1/alope) slope= -2.806 E=2.27 HIF3a-sv3 primer pair

пате	rp49 cycle#	mean	sidev	епог%,	factor
HIF3a-sv3#3	19.63	19.657	0.0929	0.47269323	1
HIF3a-sv3#3	19.76				
HIF3a-sv3#3	19.58				
HIF3a-sv3#4	19.59	19.450	0.1929	0.99163504	1.010625536
HIF3a-sv3#4	19.23				
HIF3a-sv3#4	19.63				
HIF3a-sv3#57	18.97	18.840	0.1300	0.69002123	1.043347488
HIF3a-sv3#5	18.71				
HIF3a-sv3#57	18.84				

Fig. 40: Nuclear localization of HIF3a sv3 in transgenic Drosophila

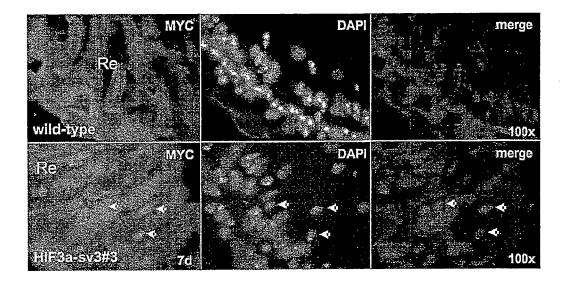


Fig. 41: HIF3a sv3 protein expression in transgenic flies

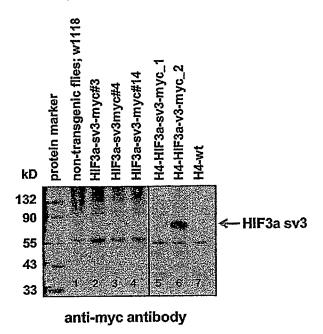


Fig. 42: HIF3a sv3 expression rescues photoreceptor cell degeneration

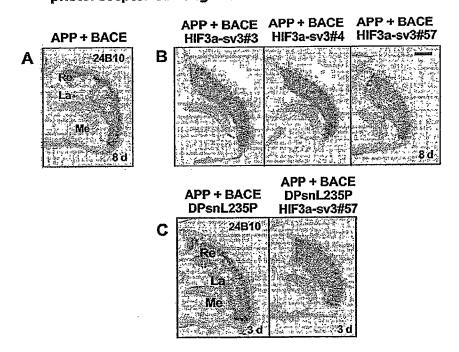


Fig. 43: Abeta level in hAPP/hBACE/HIF3a sv3 protein expressing flies

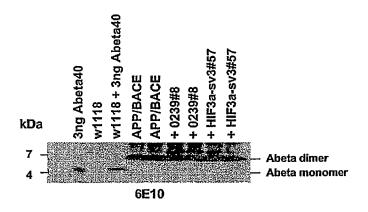


Fig. 44: Abeta plaque deposition in hAPP/hBACE/HIF3a sv3 expressing flies

